Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Ng O-T, Marimuthu K, Chia P-Y, et al. SARS-CoV-2 infection among travelers returning from Wuhan, China. N Engl J Med. DOI: 10.1056/NEJMc2003100

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Laboratory PCR for SARS-CoV-2 detection

Extraction of viral nucleic acid from respiratory specimens was performed using EZ1 virus mini kit v2.0 (Qiagen) according to manufacturer's instruction. The RNA was eluted in 60µl of AVE buffer and used as template for all assays.

Two specific real-time RT-PCR methods targeting the *N* and *ORF1ab*, were designed to detect the presence of SARS-CoV-2 in clinical samples. The *N* gene primer sequences are: forward primer 5' CTC AGT CCA AGA TGG TAT TTC T; reverse primer 5' AGC ACC ATA GGG AAG TCC. The probe sequence is: 5' FAM-ACC TAG GAA CTG GCC CAG AAG CT-BHQ1, as previously described. Thermal cycling was performed at 50°C for 20 min for reverse transcription, followed by 95°C for 15 min and then 50 cycles of 94°C for 5 s, 55°C for 1min.

The sequence for the *ORF1ab* real-time RT-PCR are: forward primer 5' TCA TTG TTA ATG CCT ATA TTA ACC; reverse primer: 5' CAC TTA ATG TAA GGC TTT GTT AAG; probe: 5' FAM- AAC TGC AGA GTC ACA TGT TGA CA-BHQ1. Thermal cycling for both *ORF1ab* was performed at 50°C for 20 min for reverse transcription, followed by 95°C for 15 min and then 50 cycles of 94°C for 5 s, 50°C for 20s and 72°C for 20s.

For both assays, a 20µl reaction containing 5µl RNA template, 500nm each of forward and reverse primer, 150nm probe and 0.2µl QuantiTect RT mix was prepared using QuantiTect Probe RT-PCR kit (Qiagen). All reactions were run on LightCycler 2.0 instrument (Roche).

All samples were also tested for endogenous RNAse P as an internal control.

Clinical features of subjects positive for SARS-CoV-2

Patient 1 reported onset of fever and cough on January 30, 2020 with only left lower zone atelectasis noted on admission chest radiograph. During her inpatient admission, she required increasing amounts of supplemental oxygen with progressive infiltrates on serial chest radiograph She was initiated on oral lopinavir-ritonavir (February 2, 2020) and electively intubated (February 6, 2020). Subsequently, her respiratory function improved with successful extubation on February 8, 2020. Repeat SARS-CoV-2 nasopharyngeal swabs were positive with the latest positive test being on February 9, 2020 (Figure S1). Subsequent tests were negative and the patient was discharged well on February 16th, 2020.

Patient 2 reported symptoms of fever and sore throat on January 30, 2020 with chest radiograph on admission revealing bilateral airspace opacification in the perihilar regions and right lower zone. She did not report close contact with a known COVID-19 case or any hospital visit in Wuhan. She required a maximum of 4L intranasal oxygen supplementation in the first five days of admission and was subsequently stable on room air. Her latest SARS-CoV-2 positive test was on February 7, 2020 with nasopharyngeal swabs on February 8 and February 9, 2020 testing negative. She was discharged well on February 10, 2020.

Patient 3, a 17-year-old male with no comorbidities, was the close contact of Patient 1, his mother. Upon direct questioning, he reported no symptoms in the two weeks prior to arriving in Singapore. Physical examination, laboratory tests and chest radiograph on admission did not reveal any abnormalities except for mild neutropenia. He did not require any supplemental oxygen and only reported mild symptoms including two episodes of diarrhea on February 7 and 8. He remains admitted in hospital as of February 19, 2020.

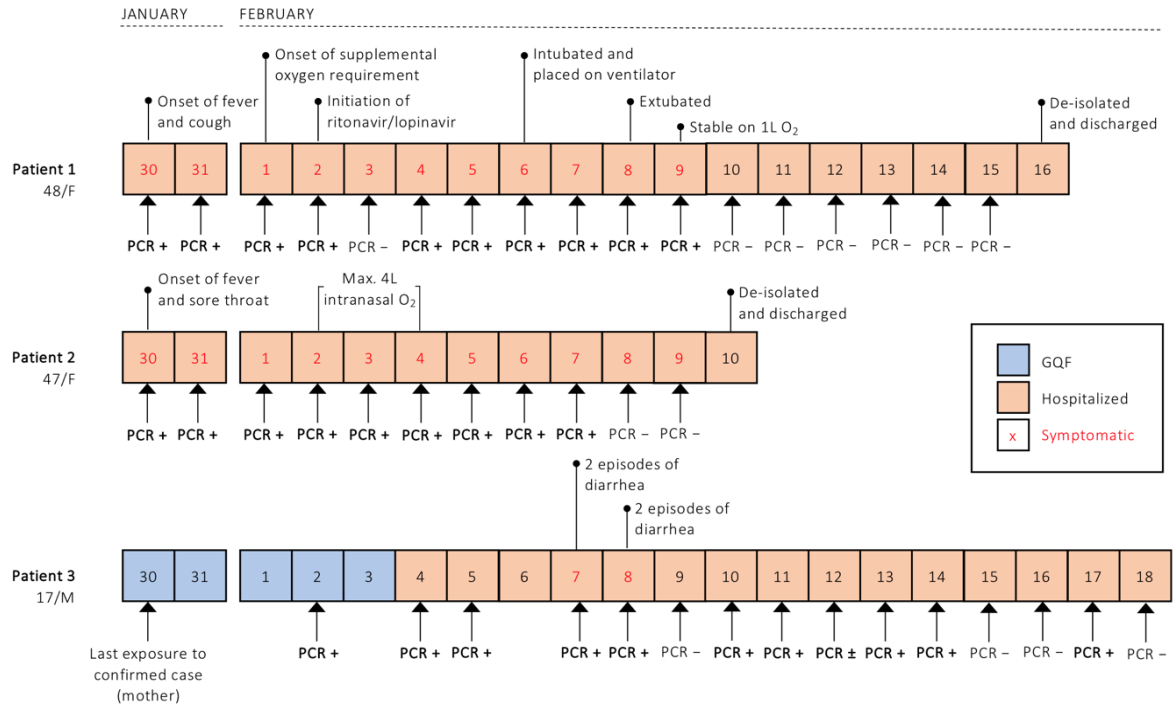

Figure S1. Chronology of symptom onset and detection of nasopharyngeal shedding of SARS-CoV-2

Estimation of point prevalence among Singaporeans evacuated from Wuhan

The variables for estimation of point prevalence among Singaporeans evacuated from Wuhan (Table S1).

Table S1. Definition of variables for estimation of point prevalence among Singaporeans evacuated from Wuhan

Notation	Interpretation. Probability of…
ι	…being *infected*, among members of the party to be evacuated
ϵ	…being symptomatic prior to arrival in Singapore if infected, i.e. *early*
λ	…being symptomatic after arrival in Singapore if infected, i.e. *late*
π	…*participating* in swabbing during quarantine

For notational simplicity we define a redundant parameter $\alpha = 1 - \epsilon - \lambda$ to be the *asymptomatic* rate. As we fit the model using a Bayesian framework, prior distributions are required for these parameters. We assume non-informative uniform priors on (0,1) for ι and π, and a non-informative Dirichlet(1,1,1) distribution for $(\epsilon, \lambda, \alpha)$. The (prospective) evacuees were partitioned into the states defined in Table S2. These states correspond to the flows described in Figure 1 in the main manuscript.

Table S2. Definition of states

State	Definition. Individuals who…
a	…were denied boarding because of symptoms present in Wuhan.
b	…developed symptoms during the flight and were isolated upon arrival in Singapore.
c	…arrived in Singapore without symptoms, participated in regular swabbing during quarantine, and did not develop symptoms or test positive
d	…arrived in Singapore without symptoms, participated in regular swabbing during quarantine, did not develop symptoms but did test positive
e	…arrived in Singapore without symptoms, was transferred to a different quarantine facility, and did not develop symptoms
f	…arrived in Singapore without symptoms, participated in regular swabbing during quarantine, and developed symptoms

From the diagram of the disposition of subjects (Figure 1), we tabulated the number of individuals n_s in state s and the probability q_s of being in that state (Table S3). Note that we merge states a and b because they are functionally the same. The data vector $(n_{ab}, n_c, n_d, n_e, n_f)$ should then follow a multinomial distribution with probabilities $(q_{ab}, q_c, q_d, q_e, q_f)$ whence the likelihood function and hence the posterior distribution is obtained.

Table S3. Number of individuals n_s in state s and the probability q_s of being in that state

State	Number	Probability
a	$n_a = 3$	-
b	$n_b = 2$	-
ab	$n_{ab} = 5$	$q_{ab} = \iota \times \epsilon$
c	$n_c = 87$	$q_c = (1 - \iota) \times \pi$
d	$n_d = 2$	$q_d = \iota \times \alpha \times \pi$
e	$n_e = 3$	$q_e = [1 - \iota + \iota \times \alpha] \times (1 - \pi)$
f	$n_f = 0$	$q_f = \iota \times \lambda \times \pi$

A Markov chain Monte Carlo algorithm was developed to sample the posterior distribution for the parameter vector, using a random walk Metropolis-Hastings proposer with bandwidths tuned on pilot runs, 1,000,000 draws with every tenth draw retained and a burn in of 100,000 iterations. Convergence was assessed visually and through running multiple chains. The algorithm was developed using R (R Core Team, 2020).

For our *baseline scenario*, we exclude the three individuals denied boarding, exclude one asymptomatic case who was the family member of an existing case and thus potentially infected through familial contact, and treat the one asymptomatic case in which a single gene target was detected as uninfected.

Table S4. Results of analysis

Parameter	Posterior mean (95% CrI), %,
ι	3.2 (0.7, 7.6)
ϵ	59.4 (19.0, 93.0)
λ	20.4 (0.6, 61.2)
α	20.2 (0.7, 60.4)

References

R Core Team (2020). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.